the optimal pattern of breathing following such an insult. Hypoxemia and pulmonary edema in the patient were quickly alleviated by mechanical ventilation with PEEP.

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Successful Treatment of Non-Meningitic Listerial Brain Abscess without Operation

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THE MOST COMMON MANIFESTATION of Listeria monocytogenes infection in the central nervous system is purulent meningitis or meningoencephalitis.[1] Focal or disseminated suppuration in the brain without meningitis is decidedly rare and only six cases have been recorded in the English literature.[2-7] We report another case of non-meningitic listeriosis with both cerebral and pulmonary abscesses. This case is also unusual in that the patient had a prolonged, relapsing illness and recovered completely without surgical intervention.

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Report of a Case (Chart 1)

A 35-year-old man with polycystic kidneys, chronic renal failure and a cadaveric renal transplant, presented in February 1971 with bilateral diffuse pulmonary infiltrates. Open lung biopsy showed acute, necrotizing bronchopneumonia. Cultures and special stains for aerobic and anaerobic bacteria, fungi, Pneumocystis carinii, and viral inclusion bodies were negative. The patient was nevertheless treated with a trial of pentamidine, penicillin, and cloxacillin. Within two and a half weeks, there was complete radiographic resolution of the pulmonary infiltrates, and he was maintained on prednisone 10 mg and azathioprine 50 mg daily.

In May 1971 he was readmitted to hospital with fever, chills, mental obtundation, expressive aphasia and right facial paresis. Meningeal signs were absent. Consolidation of the apical-posterior segment of the left upper lung was noted. There were no cardiac murmurs or evidence for peripheral embolization. Laboratory findings included hemoglobin of 8.4 grams per 100 ml, hematocrit 23.5 percent, leukocyte count 6,300 per cu mm with 16 percent neutrophils, 83 percent lymphocytes, and 1 percent monocytes, and platelet count

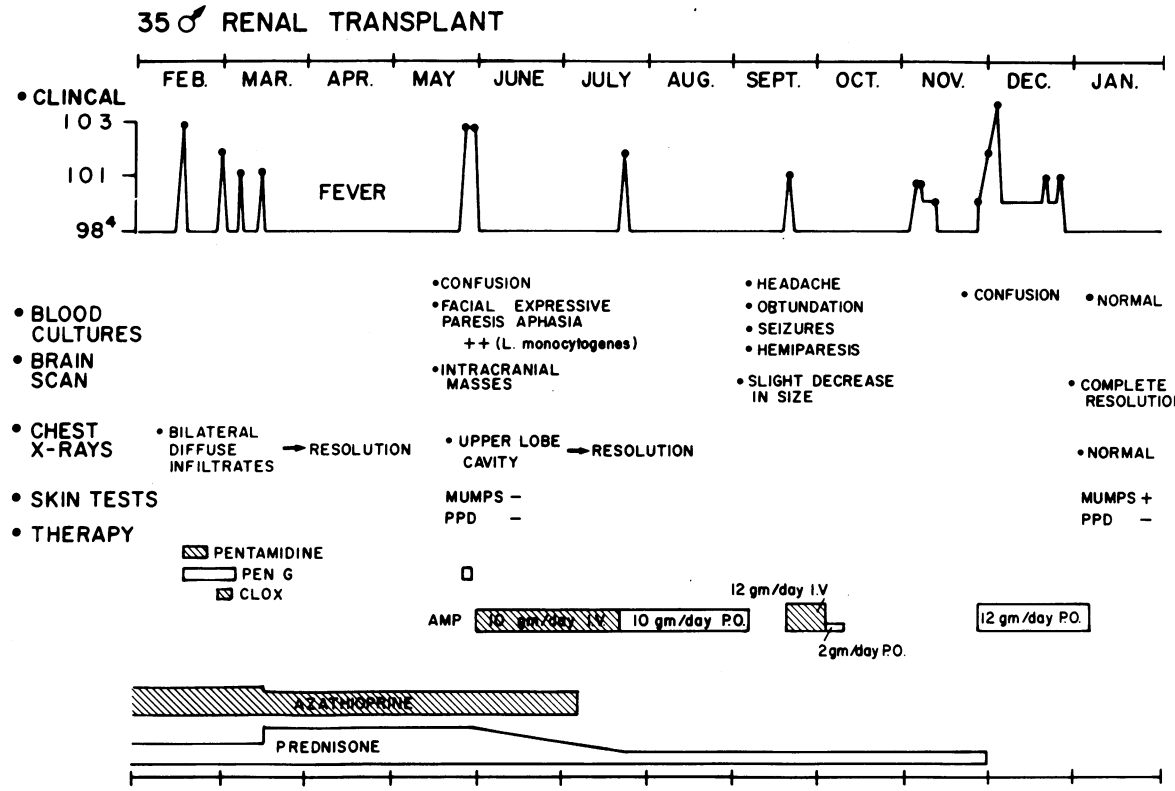

Chart 1.—Clinical course of non-meningitic listeriosis with cerebral and pulmonary abscess in a 35-year-old man following renal transplant.

of 205,000 per cu mm. Blood urea nitrogen was 80 mg and serum creatinine 4.6 mg per 100 ml. Skin tests to mumps antigen, intermediate purified protein derivative, coccidioidin, and histoplasmin were negative. The cerebrospinal fluid was clear, with an opening pressure of 150 mm of water, and contained one lymphocyte per ml with no red blood cells. Protein content was 72 mg and glucose 104 mg per 100 ml. Cultures for bacteria, fungi and viruses were negative. Blood cultures on two consecutive days, however, grew L. monocytogenes serotype la,* sensitive to penicillin, ampicillin, erythromycin, tetracycline, and chloramphenicol. X-ray films of the chest showed an abscess cavity in the left upper lung field (Figure 1), but sputum cultures were negative. Brain scans revealed two space-occupying lesions, each approximately 3 cm in diameter, deep in the left frontal and right frontotemporal regions (Figure 2). A carotid angiogram revealed a slight left to right pericallosal shift compatible with a deep left frontal mass. Because of the deep location and multiplicity of lesions, surgical drainage was not attempted. Azathioprine was discontinued and prednisone was reduced to 5 mg daily. Ampicillin, 2.5 gm every 6 hours, was administered intravenously for six weeks followed by oral therapy at the same dose for another six weeks. The fever rapidly abated and all neurological abnormalities gradually cleared. Subsequent blood cultures became sterile and the pulmonary cavitation resolved three weeks after initiation of therapy.

Two weeks after cessation of ampicillin therapy, however, the patient again complained of fever and severe bi-frontal headaches, followed by a grand mal seizure. On neurological examination, obtundation, minimal nuchal rigidity, right hemiparesis and plantar response in the right foot were noted. The cerebrospinal fluid was again clear, with no cells, and contained 38 mg of protein and 66 mg of glucose per 100 ml. The areas of increased radioisotope uptake previously described on brain scan were slightly decreased in size. There was no clinical or radiographical evidence of recurrent pulmonary involvement. Prednisone was discontinued. Although no pathogens were cultured from blood, urine, cerebrospinal fluid or sputum, recurrent listeriosis was suspected and ampicillin was given again for two weeks, followed

*Confirmed at the State of California Public Health Laboratory.

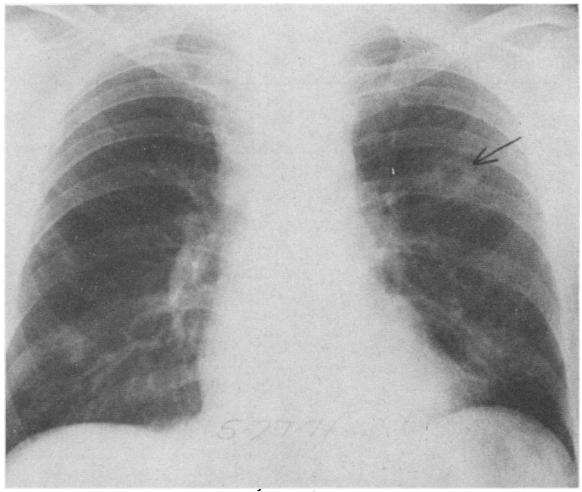

Figure 1.—Chest roentgenogram demonstrating lung cavitation in apical-posterior segment of left upper lobe.

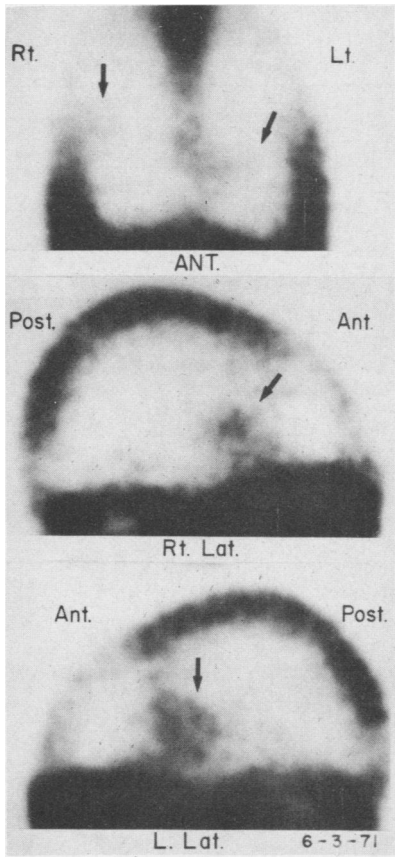

Figure 2.—Brain scans (anterior and lateral views) demonstrating two space-occupying lesions deep in the left frontal and right fronto-parietal regions.

by oral therapy for another week. As before, the fever and neurological abnormalities completely resolved.

In November and December 1971, the patient had further episodes of spiking fever and mental confusion without focal neurological signs. Cerebrospinal fluid findings and bacterial cultures were again negative. Ampicillin by mouth was given again for one month. Clinical response was good and the space-occupying lesions previously demonstrated on brain scan continued to diminish in size. They were completely resolved by January 1972. Concomitant with this resolution, the skin response to re-testing with mumps antigen became reactive. The patient thereafter remained well with no further complications.

Discussion

Focal or disseminated suppuration in the brain without meningeal involvement has rarely been attributed to L. monocytogenes. Since the initial description by Eck in 1957,[8] only six cases of non-meningitic listerial brain abscess or focal encephalitis have been reported in the English literature (Table 1). All patients presented with focal neurological abnormalities without meningeal irritation. The cerebrospinal fluid characteristically was sterile, containing less than 300 white blood cells per cu mm and was otherwise non-diagnostic. Blood cultures, on the other hand, were almost uniformly positive. As with our patient, debilitating underlying disease was present in four of the six cases and corticosteroid therapy was administered in two. Histopathologically, lesions in the brain were characterized by focal necrosis with multiple microabscesses, hyperemia, hemorrhage and perivascular cuffing.[8] Duffy et al[2] and Johnson and Colley[5] also noted extensive fibrinoid necrosis of vessel walls in the affected brain, which suggests the possibility that ischemia of surrounding tissue may interfere with adequate capsule formation in listerial brain abscess. Only one patient survived after multiple antibiotic therapy. A second patient clinically improved after surgical drainage of the brain abscess but died three months later of his underlying disease.

The diagnosis of listerial brain abscess or focal encephalitis in the case here reported, although supported by clinical, radiographical and radioisotopic evidence as well as by concurrent positive blood cultures, was nevertheless presumptive, since bacteriological confirmation of the intracranial lesions was lacking. The possibility of listerial endocarditis with septic embolization to the brain could not be completely excluded. This was unlikely, however, since there was no pre-existing heart disease or clinical evidence of valvular involvement. Pulmonary manifestations of listerial septicemia are apparently not uncommon,[1] but have hitherto been underemphasized. In three of the six cases summarized in Table 1 the pa-

TABLE 1.—*Summary of Clinical Data in Reported Cases of Non-meningitic Suppurative Encephalitis or Brain Abscess Due to L. monocytogenes*

Age, Sex	Underlying Disease	Presentation	CSF* WBC (/mm³)	CSF* L (%)	CSF* G (mg%)	CSF* P (mg%)	Culture Blood	Culture Brain	Treatment and Outcome
55[2] ♂	None	Fever, L 6th nerve palsy, Paralysis of R palate and vocal cord, bronchiolitis	183	46	95	53	+	−	Penicillin, streptomycin. Died. Autopsy: suppurative encephalitis pons and medulla, sparing of leptomeninges.
69[3] ♂	Rheumatoid arthritis treated with prednisone	Fever and headache, slurred speech, confusion, L facial paresis, diplopia and nominal aphasia	290	10	60	70	+	−	Penicillin, chloramphenicol, sulfadiazine, ampicillin. Survived with resolution of neurological abnormalities.
49[4] ♂	Rheumatic heart alcoholism and diabetes	Fever, coma, L hemiplegia and ptosis	32	..	72	106	+	−	Penicillin, streptomycin, tetracycline. Died. Autopsy: 2.5× 3.0 cm abscess with thalamus and R corpus striatum; calcified vegetations on mitral valve.
70[5] ♀	Vasculitis treated with prednisone	Fever, coma, L hemiplegia bronchopneumonia	..	..	..	..	+	+	Ampicillin, tetracycline. Died. Autopsy: multiple small abscesses, R frontal and parietal lobes.
53[6] ♂	Cirrhosis	Somnolence and disorientation, L hemiparesis	0	0	75	105	+	+	Penicillin, erythromycin. Clinical improvement following aspiration of right parietal lobe abscess. Died 3 months later of gastrointestinal hemorrhage. Autopsy not performed.
39[7] ♂	None	Headache, L hemiparesis bronchopneumonia	285	70	..	85	−	+	Therapy not specified. Died. Autopsy: small localized brainstem abscess almost transecting the upper spinal cord.

*L = lymphocytes, G = glucose, P = protein.

tients had pulmonary involvement. In the present case, pulmonary suppuration per se could have predisposed to abscesses in the brain.[9]

Until recently, intracranial suppuration without surgical intervention has been thought to be almost universally fatal. Heineman et al[10] and others,[11,12] however, demonstrated that, provided diagnosis and appropriate antibiotic therapy are established early, intracranial suppuration can be aborted or reversed without surgical intervention. This concept stemmed from Dandy,[13] who believed that, as with furunculosis, inflammation in the brain undergoes several stages, from early, poorly localized, suppurative encephalitis to a well-formed, frankly purulent abscess, with eventual encapsulation. It is believed that this early stage of "immature abscess" is reversible if the infection can be controlled by antibiotics.[14] The experience in the present case, in which antibiotic therapy was initiated within five days of neurological symptoms, appears to support this contention. However, it must be emphasized that the multiplicity and deep-seated nature of lesions in our patient precluded a surgical approach to therapy; and that in the presence of a significant mass effect, reliance on antibiotic therapy alone for well-formed brain abscess is hazardous and is not recommended.

The relapsing nature of illness without changing foci on brain scan in our patient suggests chronic low-grade infection which may have been exacerbated by immunosuppression of the host. In experimental studies involving mice, Louria et al[15] demonstrated that although mortality and tissue census of L. monocytogenes were significantly reduced, adequate doses of penicillin often did not completely eradicate the organism. MacKaness[16] further showed that progressive infection in listeriosis is related to the ability of the organism to survive and grow intracellularly and that acquired resistance is associated with the appearance of cellular immunity. It is perhaps not totally coincidental that clinical recovery in our patient was concurrent with return of cutaneous reactivity to mumps antigen.

Summary

A case of listerial brain abscess without meningitis complicating renal transplantation is reported. The relapsing nature of illness without changing foci on brain scan suggests chronic low-grade infection which may have been exacerbated by immunosuppression of the host. High-dose ampicillin therapy administered over a protracted period resulted in complete resolution of lesions without surgical intervention. This, the seventh case of non-meningitic central nervous system listeriosis to be reported in the English literature, illustrates the importance of early diagnosis and appropriate antibiotic therapy for suppurative intracranial infection.

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Disseminated Coccidioidomycosis

Diagnosis by Needle Biopsy of Liver

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MANY AGENTS produce granulomatous inflammation in the liver.[1-5] Granulomata caused by some infectious agents, such as tuberculosis or histoplasmosis, may have specific morphological features. Autopsy studies have demonstrated the spherules of Coccidioides immitis in the hepatic granulomata of patients with disseminated coccidioidomycosis,[6,7] and there are two reports of the antemortem diagnosis of hepatic granulomata due to Coccidioides immitis.[8,9]

This case of disseminated coccidioidomycosis in which spherules were seen after serial sectioning of a needle biopsy specimen of the liver demonstrates that dissemination of Coccidioides immitis may be found with low serum complement fixation titers. Therefore, liver biopsy is indicated in patients with pulmonary coccidioidomycosis and hepatomegaly or abnormal results of liver function tests even though the serum complement fixation titer is low.

Report of a Case

A 47-year-old black man was admitted to the Los Angeles County-University of Southern California Medical Center with a history of malaise, fever, chills, night sweats, and cough of two months' duration. Although he traveled to Las Vegas, Nevada from Los Angeles, California less than a week before the onset of his symptoms, his home in Northridge, California, an area well known to be highly endemic for Coccidioides immitis, was a more likely site of exposure because the incubation period for primary pulmonary disease is 10 to 14 days.[10] The symptoms persisted

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